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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,057	02/26/2002	Antoine F Carpentier	249326USOX PCT	4658

22850 7590 12/16/2005

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EXAMINER	
ZARA, JANE J	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 12/16/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,057	CARPENTIER, ANTOINE F	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-51* is/are pending in the application.

4a) Of the above claim(s) *28-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-27 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/02, 5/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Compliance Notice*.

DETAILED ACTION

This Office action is in response to the communication filed 2-14-05.

Claims 18-51 are pending in the instant application.

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. **(*e.g.* Please provide a sequence identifier (SEQ ID No.) for the sequence listed in claim 48.)** See the accompanying Notice to Comply. Applicant is requested to return a copy of the attached Notice to Comply with the reply.

Election/Restrictions

Claims 28-48 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2-14-05.

Applicant's election of Group I, claims 18-27 and 49-51 in the reply filed on 2-14-05 is acknowledged. Because applicant did not distinctly and specifically point out the

supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-27, 49-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to compositions and methods comprising immunostimulatory oligonucleotides optionally comprising modified cytosines and a medicament with anti-tumor activity, which compositions optionally additionally comprise immune system cells, cytokines, anti-tumor antibodies, tumor extracts, tumor cells or genetically modified tumor cells. The broad genera claimed, which genera include *immunostimulatory oligonucleotides comprising modified cytosines*, *medicaments with anti-tumor activities*, *immune system cells*, *cytokines*, *antitumor antibodies*, *tumor extracts*, *tumor cells* or *genetically modified tumor cells*, encompass a vast myriad of compounds, chemical structures, cells, molecules including antibodies and/or cells. Concise structural features that could distinguish structures within these genera from

others are missing from the disclosure. No common structural attributes identify the members of the claimed genera, or distinguish members within each claimed genus from those outside of that claimed genus. The specification fails to teach or adequately describe a representative number of species in each genus such that the common attributes or characteristics concisely identifying members of the proposed genera are exemplified. The specification appears to be silent regarding the incorporation of modified cytosines into the oligonucleotides. Please provide citations for such support in the application as originally filed. The specification teaches a reduction in tumor volume following administration of SEQ ID NO: 2 by various routes of administration. The specification is silent, however, regarding the disclosure of the administration of additional medicaments with anti-tumor activity. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe each of the very broad genera claimed. Thus, Applicant was not in possession of the claimed genera.

Claims 49-51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating tumors in vivo comprising the administration of immunomodulatory oligonucleotides of lengths between ~20-30 nucleobases, and comprising the octameric motif comprising AACGTTAT, does not reasonably provide enablement for methods of any cancer in vivo comprising the administration of immunomodulatory oligonucleotides of any length comprising the octameric motif comprising AACGTTAT. The specification does not enable any person

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The state of the prior art and the predictability or unpredictability of the art.

Cellular uptake by appropriate target cells is a rate limiting step that has yet to be overcome in achieving predictable clinical efficacy. Both Chirila et al and Agrawal et al point to the current limitations which exist in our understanding of the sufficient cellular uptake or tissue targeting of nucleic acid molecules in vitro and in vivo (see Agrawal et al, Molecular Med. Today, Vol. 6, pages 72-81, 2000, especially at pages 79-80; see Chirila et al, Biomaterials, Vol. 23, pages 321-342, 2002, especially pages 326-327 for a general review of the important and inordinately difficult challenges of the delivery of therapeutic molecules to target cells). The appropriate delivery of large nucleic acid molecules therefore poses a formidable rate-limiting step in providing predictable clinical efficacy. The efficacy observed for the oligonucleotides of the instant invention (e.g. less than 50 nucleobases in length) are not necessarily predictive of the efficacy of large nucleic acid molecules comprising the disclosed octameric and claimed motif.

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. The specification teaches the treatment of various tumors in mouse models following administration of immunomodulatory oligonucleotides of lengths between ~20-30 nucleobases, and comprising the octameric motif comprising AACGTTAT. Applicants have not provided adequate guidance in the specification, however, toward methods of treating any cancer, including cancers of the nervous system, comprising the administration of immunomodulatory oligonucleotides

of any lengths, and comprising the octameric motif comprising AACGTTAT. One skilled in the art would not accept on its face the examples given in the specification of the reduction of tumor growth following administration of these smaller oligomers as being correlative or representative of the ability to treat any cancer, including any nervous system cancer. There is a lack of guidance in the specification and an unpredictability associated with the successful targeting and delivery of nucleic acid molecules of any size or length in an organism, and further whereby treatment effects are provided for any cancer.

The breadth of the claims and the quantity of experimentation required. The claims are drawn to methods of treating any cancer in vivo comprising the administration of immunomodulatory oligonucleotides of any length comprising the octameric motif comprising AACGTTAT. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of a representative number of nucleic acids of varying sizes that comprise this octameric motif, and further whereby treatment effects are provided for any cancer. Other experimentation required to practice the invention claimed includes determining accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues in an organism, and which nucleic acids of varying sizes and lengths are taken up or appropriately localized in sufficient concentration, and treatment effects are provided for the broad array of cancers claimed. Since the specification fails to provide sufficient guidance for the breadth claimed, and since determination of these factors is

highly unpredictable, it would require undue experimentation to practice the invention over the scope claimed.

Allowable Subject Matter

The oligomeric sequence comprising 5' AACGTTAT 3' appears free of the prior art searched and of record.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (571) 272-0811. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the

status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jane Zara
11-23-05